· maximum intraindividual
en in the other eight subjects
nd 38% and in each of these
outpatient LDR was ≥75%
nt values. The PB indicator
each of the 11 episodes of
pliance.
raindividual variation in PB
it values ≥75% of inpatient
'good' compliance, we have
of plasma rifampicin, con-
oring compliance (Table 1).
rifampicin levels identified
f poor compliance during
identify 9 of 11 instances of
npliance. Also, no plasma
cted (< 0.5 mg l^{-1}) at five
were shown to have 'good'
B indicator. Therefore, we
ssays of plasma rifampicin
provide an effective tech-
ate identification of poor
confirmation of good com-
ereculous therapy.

ventional therapy and at

Simulated poor compliance
11
2
9 (7.7; 3.0–13.1)

88). *Thorax*, **43**, 244P.

ead to drowsiness and im-
(Nicholson, 1983, 1987).
y to be specific H1 an-
ext, we have examined the
mers of chlorpheniramine
dertness and performance.
receptors are highly stereo-
l., 1979; Borchard *et al.*,
with these drugs may help
edation can be due to H_1-
alone. Compounds were
nantiomers by fractional

crystallisation (stereoselective activity ratios > 50 on guinea-pig ileum), and their maleates encapsulated with lactose.

Six healthy volunteers (19–28 years) each ingested 10 mg of (+)- and (−)-chlorpheniramine maleate, 5 mg of (+)- and (−)-dimethindene maleate, 5 mg of triprolidine (active control), and two placebos. Treatments were arranged in a pseudo-random order balanced for linear sequence. The study was double-blind and at least 4 days separated each assessment. Sleep latencies, subjective sleepiness and digit symbol substitution were measured 1.0 h (08.30 h) before and 0.5, 1.5 and 3.0 h (10.00, 11.00 and 12.30 h) after ingestion.

Differences between changes in measures from before (08.30 h) to after ingestion were analysed between enantiomers and between drugs and placebo (see Table 1). No differences could be established at 10.00 h. At 11.00 h the reductions in sleep latencies were greater with (+)-chlorpheniramine and with (−)-dimethindene than with their respective enantiomers and with placebo. Increased subjective sleepiness was greater at 11.00 and 12.30 h with (+)-chlorpheniramine than with the (−)isomer and with placebo, and at 12.30 h with (−)-dimethindene compared with the (+)isomer. Impairment of performance was greater at 11.00 and 12.30 h with (+)-chlorpheniramine than with the (−)isomer.

As only (+)-chlorpheniramine and (−)-dimethindene, the active enantiomers, lead to drowsiness and impaired performance, it is concluded that sedation can arise from H_1-receptor antagonism alone.

Table 1

Time (h)	*Placebo*	*Triprolidine*	*Chlorpheniramine* (+)	*Chlorpheniramine* (−)	*Dimethindene* (+)	*Dimethindene* (−)
Sleep latency (min)						
08.30	26.5	27.5	20.6	19.5	21.9	23.8
11.00	12.2	3.5[b]	3.3[a,d]	10.5	8.8	3.8[a,e]
12.30	9.0	4.4	3.5	7.2	5.6	2.8
Subjective sleepiness (arbitrary units)						
08.30	2.51	2.35	2.35	2.69	2.69	2.16
11.00	2.68	3.54	3.79[a,d]	2.69	2.84	2.89
12.30	2.58	2.99	3.97[a,d]	2.52	2.63	3.28[e]
Digit symbol substitution (number of substitutions)						
08.30	248.1	244.5	245.7[c]	245.0	249.8	248.8
11.00	242.3	236.2	228.8[a]	245.5	246.3	236.8
12.30	243.6	236.0	232.0[a]	248.3	246.0	241.8

Significance levels: Comparisons with placebo – [a]$P < 0.05$; [b]$P < 0.01$
Comparisons between enantiomers – [c]$P < 0.05$, [d]$P < 0.01$

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Haemodynamic responses to food ingestion in normal human subjects before and after the somatostatin analogue, octreotide (SMS 201-995)

J. S. KOONER, S. RAIMBACH, C. WHITEHEAD, W. S. PEART & C. J. MATHIAS
Department of Medicine, St Mary's Hospital Medical School and Institute of Neurology and National Hospital for Nervous Diseases, Queen Square, London

We have investigated the haemodynamic responses to a liquid meal (60 g carbohydrate, 22 g fat, 18 g protein) in eight normal subjects before and after the somatostatin analogue, octreotide (SMS 201-995, 50 μg s.c.), which inhibits the release of gastrointestinal peptides. Non-invasive measurements of blood pressure (BP) and heart rate (HR) (Sentron), cardiac index (CI, continuous wave Doppler, Exerdop) forearm blood flow (FBF, strain gauge plethys-

mography), digital (index finger) skin blood flow (DBSF, laser Doppler flowmetry, Perimed PF2b) and superior mesenteric artery blood flow (SMABF, Duplex Scanner, Ultramark 8 ATL) were made at 10 min intervals.

After the meal, there were no significant changes in BP. There was a post-prandial increase in HR (63 ± 2 to 69 ± 2 beats min^{-1}, $P < 0.05$) and CI (430 ± 29 to 609 ± 55 cm min^{-1}, $P < 0.05$). FBF fell and forearm vascular resistance (FVR, 54 ± 6 to 74 ± 8 mm Hg ml^{-1} 100 ml^{-1} min^{-1}, $P < 0.05$) rose. DSBF and vascular resistance (DSVR) were unchanged. There was a post-prandial increase in SMABF (0.42 ± 0.05 to 0.91 ± 0.17 l min^{-1}, $P < 0.05$) and fall in superior mesenteric artery vascular resistance (SMAVR, 254 ± 44 to 134 ± 22 units, $P < 0.05$).

After octreotide there was no change in BP or other haemodynamic measurements except for a fall in SMABF (0.51 ± 0.04 to 0.36 ± 0.04 l min^{-1}, $P < 0.05$) and a rise in SMAVR (188 ± 18 to 274 ± 31 units, $P < 0.05$). Following food ingestion, there were no changes in BP and other haemodynamic measurements including SMABF (0.36 ± 0.03 to 0.34 ± 0.04 l min^{-1}, NS) or SMAVR (274 ± 31 to 290 ± 42 units, NS).

We conclude that, in normal subjects, blood pressure is maintained after food ingestion, despite a marked increase in SMABF, by compensatory changes in HR, CI and FBF. This differs from patients with autonomic failure and sympathetic denervation, in whom food substantially lowers BP, because of lack of such compensatory changes (Mathias *et al.*, 1988). Octreotide rapidly reduced basal SMABF. The haemodynamic changes induced by food ingestion, including the rise in SMABF, were prevented by octreotide, presumably by inhibiting release of peptides which induce splanchnic vasodilatation.

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POSTER COMMUNICATIONS

The effect of intradermal CGRP and histamine on blood flow in the forearm of normal volunteers and Raynaud's sufferers

S. D. BRAIN, R. G. PETTY[1], J. LEWIS[1] & T. J. WILLIAMS

Department of Applied Pharmacology, National Heart and Lung Institute, Dovehouse Street, London SW3 6LY and [1]Northwick Park Hospital and MRC Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ

Calcitonin gene-related peptide (CGRP) is present in cutaneous sensory C-fibre nerves which are in close contact with blood vessels (Gibbins *et al.*, 1977). In normal individuals intradermal CGRP induces a persistent local reddening associated with an increase in blood flow, whereas intradermal histamine induces local reddening, a wheal and surrounding axon-reflex flare (Brain *et al.*, 1985, 1986). The flare is mediated by C-fibre nerves and could therefore be due to release of CGRP. To investigate if the defect in circulatory control in Raynaud's patients is associated with a deficiency in responses to CGRP or in local axon reflexes, we have compared the response of Raynaud's patients and normal volunteers to intradermal CGRP and histamine.

The project was approved ethically and subjects gave informed consent. Raynaud's sufferers with no symptoms of scleroderma or SLE, were tested. Control volunteers were age, sex and race matched. A 1 cm^2 area of the forearm was cooled (5° C, 2 min). Normal volunteers responded with a reactive hyperaemia that was measured, after removing the cold probe, using a laser Doppler flow meter. Responses in Raynaud's patients were markedly different. Peak blood flow response: normals, before 13.2 ± 1.9% after 57.8 ± 8.4%, $P < 0.01$, paired *t*-test; Raynaud's patients, before 12.2 ± 1.9% after 28.0 ± 10.1%, NS (% flux mean ± s.e. mean, $n = 6$).

CGRP (10 pmol), histamine (500 pmol) or saline (50 µl) were injected into the volar surface of the forearm. Blood flow was measured 1 mm from injection sites for CGRP (in area of local reddening) and 10–20 mm from injection sites for histamine (in area of axon reflex flare) using a laser Doppler blood flo
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Responses in Raynaud
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Table 1
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CGRP:
(10 pmol

Table 2 T
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Saline:

Histamine
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Brain, S. D. *et al.* (1985)
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Dose-response haem in coronary disease LV dysfunction

B. SILKE, S. P. VERA
S. MAITRA & S. H. T
Departments of Car
University, and Medic
Infirmary at Leeds, Le

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